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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/777,144 | 02/13/2004 | Joseph Schlessinger | 034536-1210 | 5890 |

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

| EXAMINER | |
|---|---|
| JALLA, SANJOO | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | |

DATE MAILED: 02/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/777,144 | SCHLESSINGER ET AL. | |
| | Examiner | Art Unit | |
| | Sanjoo Shree Jalla | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *11-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**DETAILED ACTION**

1. Applicant's amendment, filed 02/13/04, is acknowledged.

   Claims 1-10 have been cancelled.
   Claims 11-13 have been added.
   Claims 11-13 are pending and under consideration in the instant application.

2. The title of the invention is not descriptive. Applicant should restrict the title to the claimed invention. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. The abstract of the disclosure is objected to because of the following informalities: The word "therefore" in the abstract reads as "therefor". Appropriate correction in spelling is required. Further, abstract of the disclosure does not adequately describe the claimed invention. Correction is required. See MPEP § 608.01(b).

4. Applicant's submission of IDS (04/27/04) is acknowledged, however references A5-A6, A9-A20, A22-A31, A33-A45, A47, A49 and A50-A64 were not located.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

   *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.*

   Claims 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

   A) The term "highly stringent condition" in claims 11 and 13 is a relative term i.e., a term who's meaning depends entirely upon the frame of reference, which renders the claim indefinite. The specification does not provide enough information as to what "highly stringent condition" encompasses i.e. the specification does not define what conditions constitute "highly stringent". One of ordinary skill in the art would not be reasonably able to establish the metes and bounds of the claimed invention.

B) Claim 11 is indefinite in the recitation of "at least a portion of" because the metes and bounds of "at least a portion of" are unclear and ambiguous. The specification does not provide enough information as to what "at least a portion of" encompasses. "at least a portion of" could be interpreted in any way. One of ordinary skill in the art would not be reasonably able to establish the metes and bounds of the claimed invention.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

An *in vitro* method for detecting in a subject the presence of a nucleic acid molecule comprising a nucleotide sequence that (i) encodes a polypeptide having the amino acid sequence SEQ ID No: 1 or SEQ ID No: 3; (ii) is the complement of the nucleotide sequence of (i); or (iii) hybridizes under highly stringent conditions comprising hybridizing at 42 °C in 50% formamide, 5X SSC, 25 mM KPO4, 5X Denhardt's, 10 ug/ml salmon sperm DNA and 10% sulfate followed by washing at 58 °C in 0.1X SSC and 0.1% SDS to the nucleic acid molecule of (i) comprising: (a) contacting a cell from said subject with a nucleic acid probe comprising nucleic acid molecule of (i) or (ii) under highly stringent conditions wherein said probe would hybridize to its complement sequence; (b) measuring the hybridization of said probe to the nucleic acid molecules of said cell or a nucleic acid extract thereof, thereby detecting the presence of said nucleic acid molecule.

Does not reasonably provide enablement for:

A method for detecting in a subject the presence of a nucleic acid molecule comprising a nucleotide sequence that (i) encodes a polypeptide having the amino acid sequence SEQ ID No: 1 or SEQ ID No: 3; (ii) is the complement of the nucleotide sequence of (i); or (iii) hybridizes under highly stringent conditions to the nucleic acid molecule of (i) or (ii), comprising:

(a) contacting a cell or an extract thereof from said subject with a nucleic acid probe comprising at least a portion of the nucleic acid molecule of (i), (ii), or (iii) under highly stringent conditions;
(b) measuring the hybridization of said probe to the nucleic acid molecules of said cell or an extract thereof, thereby detecting the presence of said nucleic acid molecule (claim 11).

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art". The " amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses at page 57, hybridization as a part of a Northern Analysis in an example. Hybridization technique is well known in the art where base pairs are formed between complementary regions of two strands of DNA that were not originally paired. However, there does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make a probe that would hybridize

to both sense and antisense strands of cDNA i.e. hybridize to nucleic acid sequence as well as its complement as claimed in claim 11 (iii). Further a nucleic acid probe comprising at least "a portion" of the nucleic acid molecule is claimed. "A portion" of nucleic acid would include oligonucleotides that would not bind under high stringency conditions as well. It is well known in the art (see in particular, Ausubel et.al. Current protocols in Molecular Biology, UNIT 6.4 Using Synthetic Oligonucleotides as *Probes)* that if oligos shorter than 17 bases are used, the general background will be higher i.e. sensitivity will be lower therefore, under highly stringent conditions where the temperature is high and salt concentration is low, oligos with 1 or 5 base pairs will not hybridize as well. Since "a portion of" nucleic acid molecule would encompass oligonucleotides with 1 or 5 or 15 base pairs, these would have reduced sensitivity and the hybrids would be less stable because of the short length of the probes. Therefore, recitation of "a portion of" does not allow the skilled artisan to make and use the hybridizing nucleic acids commensurate in scope with the instant claims without undue experimentation.

The claim further recites contacting a "cell or extract thereof" in step a) of the claimed method for detecting in a subject the presence of a nucleic acid. The claims recite no limitation that the cell extract would have DNA. Additionally, DNA present in the cell extract could be destroyed or denatured during the extraction procedure. In that case the probe would not be able to detect it. Further, as written in claim 11, "A method for detecting in a subject the presence of a nucleic acid molecule", the method could be an *in vivo* method but the claim in section (a) of claim 11, further reads "under highly stringent conditions". One can generate highly stringent conditions *in vitro* but not in vivo. Therefore, one skilled in the art will not know how to apply high stringency conditions of *in vitro* to *in vivo* method. Further, if the method is *in vivo*, cell isolation step is missing and also it is not clear how the cell is prepared for contacting with a nucleic acid probe. In absence of all this information a skilled artisan cannot perform the method commensurate in scope with the instant claims without undue experimentation.

7. Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following written description rejection is set forth herein. This is a New Matter rejection for the following reasons:

Applicant's amendment, filed 02/13/04 asserts that no new matter has been added and it directs support to pages 9, lines 2-11 (claim 11), page 9, lines 12-13 (claim 12), and page 57, lines 4-9 (claim 13), for the written description of claims 11-13. The specification and the claims as originally filed do not provide support for the invention as claimed, specifically:

A) A method for detecting in a subject the presence of a nucleic acid molecule comprising a nucleotide sequence that (i) "encodes a polypeptide having the amino acid sequence SEQ ID No: 1 or SEQ ID No: 3;" (ii) is the complement of the nucleotide sequence of (i); or (iii) "hybridizes under highly stringent conditions to the nucleic acid molecule of (i) or (ii)", comprising:
(a) contacting a cell or an extract thereof from said subject with a nucleic acid probe comprising at least a portion of the nucleic acid molecule of (i), (ii), or (iii) under highly stringent conditions;
(b) measuring the hybridization of said probe to the nucleic acid molecules of said cell or an extract thereof, thereby detecting the presence of said nucleic acid molecule (claim 11).

B) The method of claim 11, additionally comprising before step (a): selectively amplifying said nucleic acid molecule of (i), (ii), or "(iii)" (claim 12), i.e. the limitations of claim 12 as applied to the method of claim 11.

C) "The method of claim 11 or 12, wherein highly stringent conditions comprise hybridizing at 42 °C in 50% formamide, 5X SSC, 25 mM KPO4, 5X Denhardt's, 10 ug/ml salmon sperm DNA and 10% sulfate followed by washing at 58 °C in 0.1X SSC and 0.1% SDS"(claim 13).

A review of the specification fails to reveal support for the new limitations.

Regarding A), at page 9, the specification discloses that the invention is also directed to a method for detecting the presence of nucleic acid encoding a "normal or mutant RPTP" in a subject comprising: (a) contacting a cell or an extract thereof from the subject with an oligonucleotide probe encoding at least a portion of the normal or mutant RPTP under hybridizing condiitons; and (b)

measuring the hybridization of the probe to the nucleic acid of the cell, thereby detecting the presence of the nucleic acid. The specification does not appear to disclose a method for detecting the presence of nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide having the amino acid sequence SEQ ID No: 1 or SEQ ID No: 3 as now recited in the claim. The specification does not disclose normal or mutant RPTP to be the same as polypeptide having the amino acid sequence SEQ ID No: 1 or SEQ ID No: 3. Further, the specification does not disclose a method for detecting in a subject the presence of a nucleic acid molecule comprising a nucleotide sequence that hybridizes under highly stringent conditions to the nucleic acid molecule of (i) or (ii).

Regarding B), at page 9, the specification discloses that the DNA can be selectively amplified, using the polymerase chain reaction, prior to assay. The specification does not appear to disclose an additional method step where nucleic acid molecule of (i), (ii) or (iii) is amplified.

Regarding C), at page 57, the specification discloses hybridization as a part of a specific Northern Analysis in a specific example. The specification does not disclose a generic method comprising the limitations of the method for detecting a nucleic acid as claimed in claims 11 and 12.

8. Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has disclosed a nucleic acid probe comprising "at least a portion of" (claim 11). The skilled artisan cannot envision what exactly the applicant means by "at least a portion of" in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of

a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features that are common to the genus. That is, the specification does not provide a representative number of species (i.e. number of nucleotides in the probe) to describe the claimed genus, nor does it provide a description of structural features that are common to species (at least a portion of). Specification does not define the structure or function of the probe comprising "at least a portion of" the nucleic acid molecule. The probes comprising "at least a portion of" nucleic acid molecules could encompass any length of nucleic acid molecules for example it could be 5 nucleotide long or 15 nucleotide long or 1 nucleotide long. These portions clearly have different structure and if the probe is small length probe then it might have higher non-specific binding. Further, the disclosure provides an insufficient description of this essentially unlimited genus (at least a portion of).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sanjoo Jalla whose telephone number is (571) 272-4453. The examiner can normally be reached Monday through Friday from 8:00 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-

0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sanjoo Jalla, Ph.D.
Patent Examiner
Technology Center 1600

2/6/09
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER